Docket No.: 20052/1200517-US3
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:
Randolph J. Noelle

Confirmation No.: 2231

Application No.: 09/467,317

Art Unit: 1644

Filed: December 20, 1999

Examiner: P. Gambel

For: USE OF ANTIBODIES THAT SPECIFICALLY BIND CD40CR (CD40 LIGAND) TO INHIBIT HUMORAL IMMUNITY

DECLARATION OF RANDOLPH J. NOELLE UNDER 37 C.F.R. § 1.131

MS Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

I, Randolph J. Noelle, hereby declare and state that:

1. I am a U.S. citizen and am more than twenty-one years of age.

2. I am the inventor of the invention claimed in the above-captioned patent application ("the '317 application").

3. I re-affirm my duty of candor and good faith in dealing with the United States Patent and Trademark Office ("USPTO"), including the duty to disclose to the USPTO all information known to be material to the patentability of the invention as defined in 37 CFR §1.56.

4. I have read and am familiar with the '317 application as it was filed in the U.S. Patent and Trademark Office and the pending claims.

5. I have read and am familiar with the Lederman patent (U.S. Patent No. 5,993,816). I understand that the Lederman patent is based on an application filed November 15, 1991, and that it has been cited against the '317 application. I am submitting this declaration to antedate the Lederman patent.

6. Prior to November 15, 1991, the effective date of the Lederman patent, I had conceived the invention as described and claimed in the '317 application.

7. The invention was diligently reduced to practice in my laboratory and under my supervision and control.

8. The documents submitted as Exhibit A are pages from laboratory notebooks maintained in the laboratory where the invention of the '317 application was created. These pages show the results of a screen of monoclonal antibodies to identify a monoclonal antibody capable of binding CD40CR (now also known as CD40 ligand, CD40L, gp39, 5c8 antigen, TBAM, and CD154).

9. The experiment behind this screen was conducted as follows. Briefly, splenocytes from hamsters immunized with activated T cells were fused with NS1 mouse myeloma cells to produce hybridomas. Supernatants from these cultured hybridomas were screened by flow cytometry for reactivity with resting and activated T cells. Antibodies that recognize activated but not resting T cells could produce an antibody useful for inhibiting activated T cell induction of B cell activation.

10. The notebook pages of Exhibit A identify a hybridoma that selectively reacted with activated T cells. The antibody secreted by this hybridoma is the MR1 anti-CD40CR antibody as described in the specification. I understand that this hybridoma has been made publicly available at the American Type Culture Collection via ATCC Accession No. HB 11048. The first notebook page is a photocopy of the tissue culture plate in which this screen was conducted. The second notebook page identifies

the flow cytometry results for each hybridoma tested in this screen. These pages identify the MR1 antibody in the well of column 1, row 2, labeled as "20C8" on the plate.

11. MR1 is described in the specification of the '317 application. This antibody inherently possesses the recited properties of an antibody that binds an antigen that: (a) is present on activated but not resting T-cells; (b) has the same molecular weight as a protein precipitated by a CD40-immunoglobulin fusion protein (CD40-Ig); and (c) is pre-cleared by precipitation with the CD40-Ig. This antibody further blocks binding of the CD40-Ig to activated T-cells and inhibits T-cell induction of B-cell activation. An antibody having these properties can be used in methods to inhibit immunoglobulin production, inhibit activation of B cells, and treat autoimmune conditions. Thus, these pages show an antibody that has all of the characteristics of the claimed invention.

12. Under my direction and supervision, my laboratory worked continuously and diligently on the subject matter of the invention from just prior to the filing date of the Lederman patent on November 15, 1991, until the filing of the priority U.S. Application No. 07/835,799 on February 14, 1992.

13. I declare further that statements made in this declaration of my own knowledge are true and that all statements made on information and belief are believed to be true and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing therefrom.

Date: 9/29/05

Randolph J. Noelle

Screen 7 -

Screen 7

	1	2	3	4	5	6	7	8	9	10	11	12
A	33/22 44/10	8.4/12 7.5/15	32/11 84/23	25/25 26/28	90/39 90/42	97/33 99/38	6.5/10 6.9/12	8.4/10 7/9	26/24 38/33	9/13 16/11	4.9/10 2.9/11	6/10 3/11
B	9.6/11 81/22	90/30 91/35	5/15.5 88/27	72/16 91/34	10.7/10.7 10/11.	23/17 62/16.	5/10 12/10	15/13 23/13	90/107 97/77	3.9/11.0 4/100	04/20 20/24	56/24 94/30
C	5.9/12 25/25	6/12 -78/20	41/24 39/31	4/14 3.5/11	95/30 92.7/42	4.3/10.4 4/11.	93/10 98/31	99/82.1 98/95	97/42 28/32	14/11 23/11	94/82 97/209	17/14 30/17
D	42/15 52/16											
E												
F												
G												
H												

PD AGAIN

-VE = 3.3/8.9.

CD3 = 66.6/15.9.

α/β = 26.5/11.0.